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Microsystem for label-free detection of chromosomal translocations

Dorota Kwasny[1], Birgitte Bertelsen[3], Maria Dimaki[1], Asli Silahtaroglu[2], Zeynep Tumer[3], Winnie E. Svendsen[1]

(1)Technical University of Denmark, Department of Micro- and Nanotechnology, Kgs. Lyngby, Denmark
(2) University of Copenhagen, Faculty of Health Sciences, Department of Cellular and Molecular Medicine, Copenhagen, Denmark
(3) The Kennedy Center, Center for Applied Human Molecular Genetics, Glostrup, Denmark
dorota.kwasny@nanotech.dtu.dk

Congenital disorders and malignancies are often associated with chromosomal translocations. Accurate and rapid detection of chromosome abnormalities is essential for diagnosis, prognosis, management, treatment and the follow-up of the patients. The current cytogenetic analyses include chromosome banding and fluorescence in situ hybridization, but these techniques either require complex and expensive systems, specialized expertise, or prior knowledge of the karyotype. Furthermore, obtaining metaphase chromosome spreads from cancer cells is troublesome and the spreads have poor quality. Therefore, it is necessary to develop a novel system using bio-/micro-/nanotechnology that would enable rapid, reliable and automatic detection of unknown chromosomal translocations. The prototype of such a microsystem is presented here, designed to detect a translocation between chromosome 8 and 20 with a known breakpoint.

The developed prototype of the microsystem contains an array of electrodes and chambers for loading probes and target DNA sample. The chambers are coated with chromosome 8 and 20 specific probes, which are immobilized on the electrode surface via thiol-gold self-assembly. This assembly can withstand the elevated temperature necessary for the hybridization experiment. Electrochemical impedance spectroscopy is performed to enable detection of the hybridization event between the immobilized probes and the chromosomal fragments. The first step in the development of the system is to successfully hybridize long DNA fragments in suspension to surface probes. The fragment hybridized to one of the chambers is further released and allowed to hybridize to another chamber with probes targeting the second chromosome. A positive signal in the second chamber will indicate the presence of a derivative chromosome.

Further development of a microsystem with 24 chambers coated with probes that specifically target all human chromosomes will allow determination of specific key-lock combination for each chromosome translocation. The system will also enable isolation of the derivative chromosomes for further analysis with e.g. next generation sequencing.